IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 6 Ver. IV (Jun. 2015), PP 44-47
www.iosrjournals.org

Role of Interleukins in the Prognosis of Cancer

Dr.Reshma Prakash Chavan

Abstract: *Tobacco products are known carcinogens. Chemicals presents in the tobacco products are poisonous and addictive. Interleukins synthesized by helper CD4, T lymphocytes, monocytes, macrophages, and endothelial cells are markers of malignancies. Interleukins can be utilized for markers of immune system activation in prognosis of cancer. The present study was designed to study and correlate oxidative stress markers IL6, 8 and MDA in the different tobacco consumption pattern with benign and malignant conditions in male and female population.*

Keywords: *Interleukins, Tobacco, carcinogens.*

I. Introduction

Tobacco products are divided into smoking in the form of bidis, cigarettes, shisha, hookah and smokeless tobacco. Smokeless tobacco is available in the two forms chewing tobacco and snuff. Snuff is a powdered tobacco. Smokeless tobacco is used in the form of flavoured varieties of gutkha and pan masalas. The chemicals contained in chew or snuffs are poisonous and addictive. In India, 86% tobacco is used for smoking, 13% is used as chewing tobacco and 1% as snuff. (1)

Interleukins synthesized by helper CD4, T lymphocytes, monocytes, macrophages, and endothelial cells are markers of malignancies. Interleukins can be utilized for markers of immune system activation in prognosis of cancer. Interleukins may stimulate cancer cells growth. Elevated serum cytokine level was observed in the study done by Kozłowski L, et al. in 2003 in serum of breast cancer patients. As per the study done by Kawabata T, et al. in 2001 interleukin-18 was used as biomarker for gastric carcinoma. IL-6, IL-12, IL-15, IL-17 levels were altered in cancerous conditions of different parts of body. (2)

Rhodus NL, et al. had studied the difference in the salivary level of TNF-α, IL-1α, IL-6, and IL-8, using ELISA, to differentiate between malignant and premalignant lesions, in comparison to healthy subjects. (3)

Study done by Katakura A, et al. in 2007 had shown that ELISA has also been used to compare the levels of IL-1β, IL-6, IL-8, and osteopontin in cell-free saliva collected from 19 OSCC patients and 20 controls. The results showed significant difference of IL-6 between the two groups. (4) Study done by Duffy SA, et al in 2008 had suggested salivary interlukin-6 as a predictor of survival and prognosis of patients with OSCC. (5)

Aims and Objective-

The present study was designed to study and correlate oxidative stress markers IL6, 8 and MDA in the different tobacco consumption pattern with benign and malignant conditions in male and female population. Our aim was to study whether there is correlation between development of ENT diseases like oral sub mucus fibrosis, stomatitis, and gingivitis, leukoplakia, erythroplakia, carcinoma and these biochemical parameters.

II. Material And Methods

In this study tobacco consuming patients were selected. Control group was healthy with no addiction to tobacco, alcohol etc. Tobacco consumption in the form of tobacco, tobacco with lime, tobacco consumption in the pan (quit), tobacco mishari application on teeth, tobacco smoking in the form of bidis and cigarettes, ghutka, mawa, jerda, tobacco used as snuff, etc. all were included. Patients included in this study population consumed tobacco products daily for more than 2 years duration. The selection of patients was done at random. Clinical examination of patients was done which included ear, nose, and throat examinations. Informed consent was taken before the blood investigations.

Inclusion criteria-

1. Tobacco consumers with benign and malignant ear, nose, throat lesions between the age group 15 yrs to 60 yrs.
2. Non tobacco consumers without ear, nose, throat diseases between the age group 15 yrs to 60 yrs.
3. Patients using tobacco in the smoking and or chewing form with occasional alcohol drinker.

Exclusion criteria:-

1. Patients with diabetes mellitus, hypertension, pancreatic diseases, liver diseases, kidney diseases, heart diseases and H.I.V positive patients.

2. Patients with upper and lower respiratory tract infection and known genetic disorders.

Blood collection

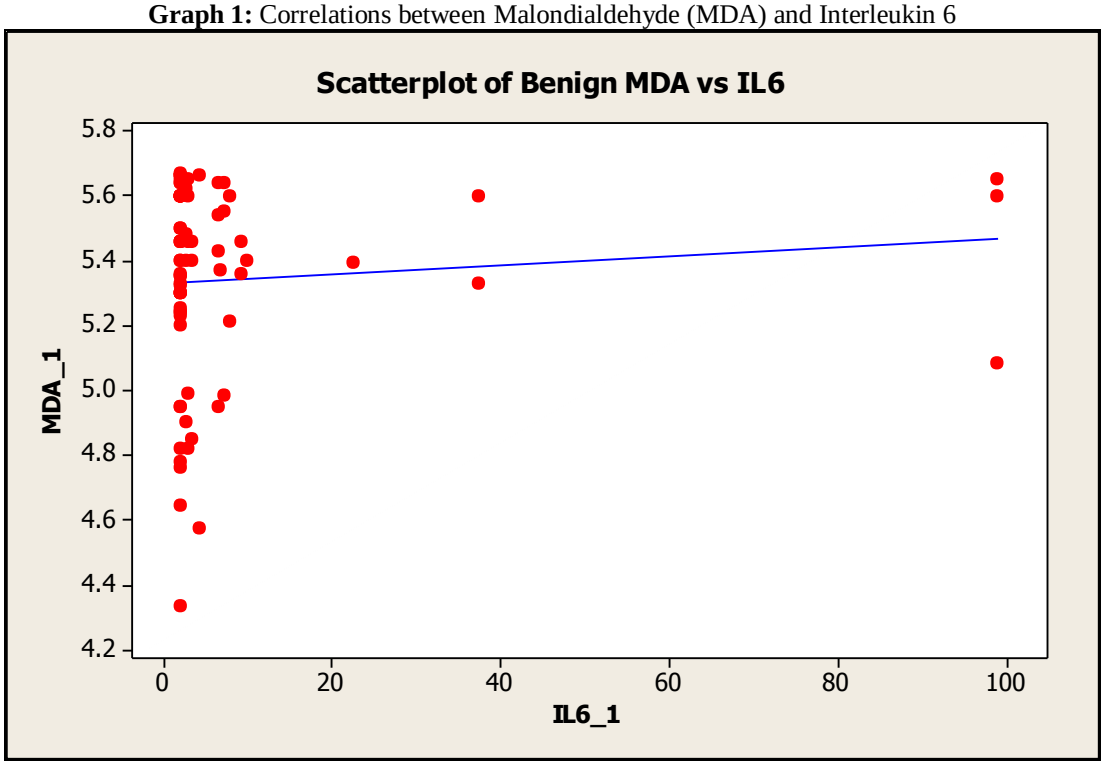
Venous Blood samples were collected after overnight fasting from the antecubital fossa by venipuncture using a 20-gauge needle with 2-ml syringe and immediately transferred to the laboratory. The blood sample was allowed to clot at room temperature and after 1 hour serum was separated from blood by centrifuging at 3000rpm for 5 min. All samples were stored in deep freezer under -70^0 C temperature and the estimations of the study parameter were carried out. MDA by Buege and Aust using spectrophotometer JASCO 670 and IL6, IL-8 by IMMULITE 1000 Analyzer (Siemens Medical Solutions Diagnostics)

Observations-

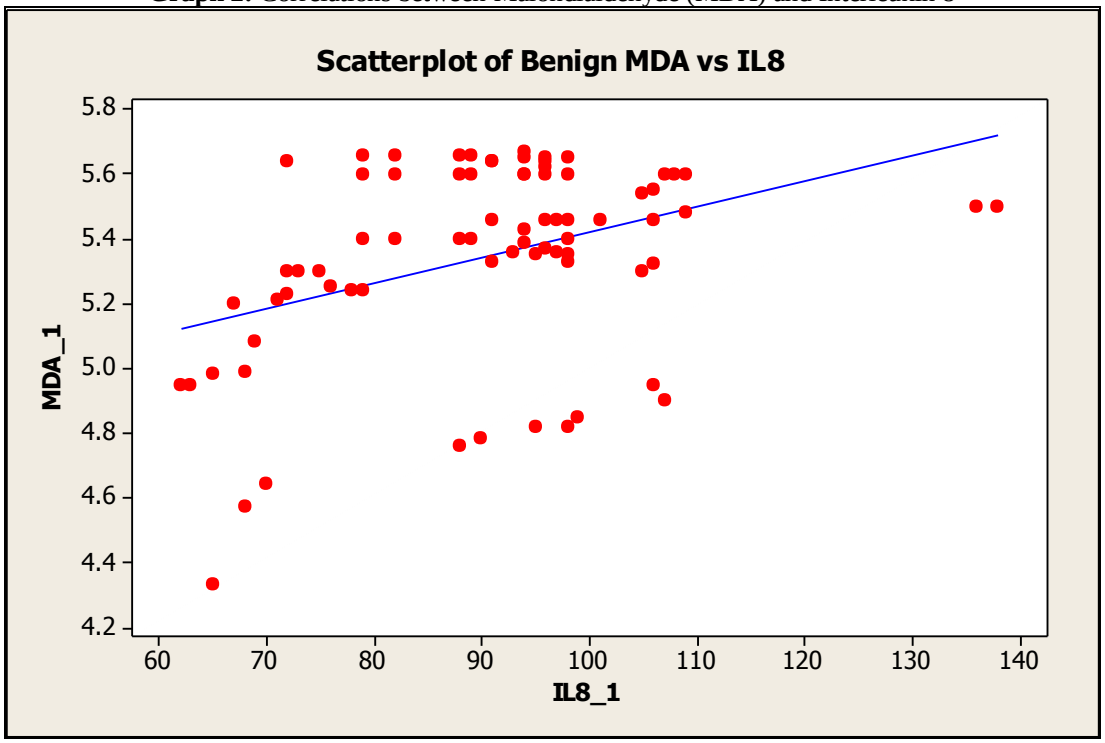
Table 1:- Tobacco consumption pattern and level of Malondialdehyde (MDA), IL6, IL8 in the patients with benign and malignant lesion

	IL6 (Mean±SD)	IL8 (Mean±SD)	MDA (Mean±SD)
Benign Group			
Smoking (n=25)	5.89±3.25	79.24±28.28	4.99±0.69
Smoking+chewing(n=25)	6.77±0.22	92.64±8.48	5.41±0.155
Smoking+chewing+Alcohol(n=25)	12.21±3.733	99±0.71	5.62±0.085
Cancer Group			
Smoking (n=25)	23.65±0.424	736.456±555.79	7.77±0.71
Smoking+chewing(n=25)	24.42±40.44	772.50±301.23	8.59±0.19
Smoking+chewing+Alcohol(n=25)	82.24±3.46	1961.92±583.36	8.75±0.21

Graph 1: Correlations between Malondialdehyde (MDA) and Interleukin 6



Graph 2: Correlations between Malondialdehyde (MDA) and Interleukin 8



III. Results

MDA level increases in tobacco induced increased oxidative stress. In present study interlukin 6 and interlukin 8 levels were significantly increased in benign group and malignant group as compared to control group (Table 1). MDA is the marker of oxidative stress is increased in both benign and malignant Otorhinolaryngological conditions. There is significant positive correlation (Table 2) between Malondialdehyde (MDA) and interleukins in the malignant ENT lesions. In the present study, Interleukin 6 and 8 both was increased in the diseased conditions, more in the malignant lesions. MDA, marker of oxidative stress was also increased along with the interleukins in diseased states. MDA, IL-6, IL-8 all values were increased in benign and malignant Otorhinolaryngological conditions.

IV. Discussion

Tobacco consumption in any form would increases oxidative stress. Study done by Dhouha Haj Mouhamed, et al had shown significant increase in MDA in smokers. There was a positive significant correlation between MDA and number of cigarettes smoked/day. [(6)] Lykkesfeldt J, et al (2004) had shown the effect of smoking in a cohort of smokers and non-smokers with similar antioxidant profiles. The smokers had significantly higher plasma levels of MDA with no difference in antioxidant status. [(7)]

Interleukins are synthesized by helper CD4 T lymphocytes, monocytes, macrophages, and endothelial cells. Cytokines such as epidermal growth factor, interleukins-6 and -8, vascular endothelial growth factor, interleukins 4 and 10, tumour necrosis factor and endothelin are well studied for target therapy for OSCC. [(8)] Elevated IL-6, IL-8, and IL-10 serum concentration were strongly associated with breast cancer. [(9)] Sato et al. [(10)] was found significantly increased interleukin (IL)-6 levels in saliva of oral cancer patients than controls. Brailo et al. [(11)] had shown significantly higher levels of salivary IL-6 and tumour necrosis factor alpha (TNF-α) in patients with oral leukoplakia. Saliva of patients with periodontitis had shown increased levels of IL-6 and IL-8. [(12)] The study done by Arellano-Garcia, et al (2008) had proven that Patients with periodontitis had higher levels of IL-8 and IL-1beta and much greater levels in patients with OSCC. [(13)] Several studies have showed elevated levels of pro-inflammatory cytokines IL (IL-6, IL-12, IL-15, and IL-17) in various malignancies. [(14)]
Duffy SA (2008) had shown that the level of salivary IL-6 could be used as marker for mortality and treatment outcome. [(15)]

MDA is the marker of oxidative stress is increased in both benign and malignant Otorhinolaryngological conditions. In the present study, Interleukin 6 and 8 both was increased in the malignant lesions [(12)] MDA, marker of oxidative stress was also increased along with the interleukins in diseased states. MDA, IL-6, IL-8 all values were increased in benign and malignant Otorhinolaryngological conditions. MDA,

IL-6, IL-8 were increased more in the malignant Otorhinolaryngological conditions. [6, 9, 10, 12] There is significant positive correlation (Table 2) between Malondialdehyde (MDA) and interleukins in the malignant ENT lesions. MDA level increases in tobacco induced increased oxidative stress.

V. Conclusion

Elevated levels of IL-6 and IL-8 have seen in the patients with benign and malignant Otorhinolaryngological lesions. There is significant positive correlation between Malondialdehyde (MDA) and interleukins in the malignant ENT lesions.

References

[1]. Mehta FS, Hamner JE. Tobacco-related oral mucosal lesions and conditions in India - A guide for dental students, dentists and physicians. Bombay: Basic dental research institute, Tata Institute of fundamental research; 1993.
[2]. Yanbaeva DG, Dentener MA, Creutzberg EC, Wesseling G, Wouters EF. Systemic effects of smoking. Chest 2007; 131 : 1557- 66.
[3]. SahebJamee M, Eslami M, AtarbashiMoghadam F, Sarafnejad A. Salivary concentration of TNF-alpha, IL-1alpha, IL6, and IL8 in oral squamous cell carcinoma. Med Oral Patol Oral Cir Bucal 2008; 13: E292-5.
[4]. Rhodus NL, Ho V, Miller CS, Myers S, Ondrey F. NF-kappaB dependent cytokine levels in saliva of patients with oral preneoplastic lesions and oral squamous cell carcinoma. Cancer Detect Prev 2005; 29:42-5.
[5]. Katakura A, Kamiyama I, Takano N, Shibahara T, Muramatsu T, Ishihara K, et al. Comparison of salivary cytokine levels in oral cancer patients and healthy subjects. Bull Tokyo Dent Coll 2007; 48:199-203.
[6]. Dhouha Haj Mouhamed, Asma Ezzaher, Fadoua Neffati, Lotfi Gaha,Wahiba Douki and Mohamed Fadhel Najjar .Effects of Cigarette Smoking on Oxidative Stress Biomarkers (pp.155-180)
[7]. Lykkesfeldt J, Viscovich M, Poulsen HE. Plasma malondialdehyde is induced by smoking: a study with balanced antioxidant profiles. Br J Nutr. 2004; 92(2):203-6.
[8]. Z. Culig, "Interleukin-6 as a therapy target in oral squamous carcinoma," Expert Opinion on Therapeutic Targets 2013; 17(1): 53–59.
[9]. Kozłowski L, Zakrzewska I, Tokajuk P, Wojtukiewicz MZ. Concentration of interleukin-6 (IL-6), interleukin-8 (IL-8) and interleukin-10 (IL-10) in blood serum of breast cancer patients. Rocz Akad Med Bialymst. 2003; 48:82-4.
[10]. Sato J, Goto J, Murata T, Kitamori S, Yamazaki Y, Satoh A, et al.Changes in saliva interleukin-6 levels in patients with oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010; 110:330–6.
[11]. Brailo V, Vacicevic-Boras V, Cekic-Arambasin A, Alajbeg IZ,Milenovic A, Lukac J. The significance of salivary interleukin 6and tumor necrosis factor alpha in patients with oral leukoplakia.Oral Oncol. 2006; 42:370–3.
[12]. Giannopoulou C, Kamma JJ, Mombelli A. Effect of inflammation, smoking and stress on gingival crevicular fluid cytokine level. Journal of Clinical Periodontology. 2003; 30(2):145–153.
[13]. Arellano-Garcia ME, Hu S, Wang J, et al. Multiplexed immuno bead-based assay for detection of oral cancer protein biomarkers in saliva. Oral Diseases. 2008; 14(8):705–712.
[14]. Kawabata T, Ichikura T, Majima T, Seki S, Chochi K, Takayama E, et al. Prospective serum interleukin-18 level as a postoperative prognostic marker in patients with gastric carcinoma. Cancer. 2001; 92:2050–5.
[15]. Duffy SA, Taylor JM, Terrell JE, Islam M, Li Y, Fowler KE, et al. Interleukin-6 predicts recurrence and survival among head and neck cancer patients. Cancer 2008; 113:750-7.